If the Examiner believes that a telephone conference would be of value, he is requested to call the undersigned attorney at the number listed below.

Any additional fees required in connection with this submission may be taken from Merck Deposit Account No. 13-2755.

Respectfully submitted,

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231, on the date appearing below.

MERCK & CO., INC.

By _____ Date 1/8/03

Date: 12/19/02

By _____
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Version Showing Markings of Pending Claims

1. (Amended) A synthetic polynucleotide comprising a sequence encoding a codon-optimized human papillomavirus serotype 16 (HPV16) protein, or mutated form thereof [a HPV protein] which has reduced protein function for viral replication and cellular transformation as compared to wild-type protein, but which maintains immunogenicity, wherein said polynucleotide sequence comprises[ing] codons that are optimized for expression in a human host.

2. A polynucleotide according to Claim 1 wherein the protein is selected from the group consisting of: L1, L2, E1, E2, E4, E5, E6 and E7.

3. A polynucleotide according to Claim 2 wherein the protein is selected from the group consisting of: L1, E1, E2, and E7.

4. A polynucleotide according to Claim 2 which is DNA.

[5. A polynucleotide according to Claim 4 wherein the protein is L1 and is from an HPV selected from the group consisting of: HPV6a, HPV6b, HPV11, HPV16, HPV18, HPV31, HPV33, HPV35, HPV39, HPV45, HPV51, HPV52, HPV56, HPV58, and HPV68.]

6. (Amended) A polynucleotide according to Claim [5] 4 wherein the protein is an HPV16 L1 protein.

7. A polynucleotide according to Claim 6 which comprises the polynucleotide of FIGURE 1 (SEQ.ID.NO: 1).

[8. A polynucleotide according to Claim 4 wherein the protein is an E1 protein or a mutated E1 protein and is from an HPV selected from the group consisting of: HPV6a, HPV6b, HPV11, HPV16, HPV18, HPV31, HPV33, HPV35, HPV39, HPV45, HPV51, HPV52, HPV56, HPV58, and HPV 68.]

9. (Amended) A polynucleotide according to Claim [8] 4 wherein the protein is a mutated form of E1.

10. (Amended) A polynucleotide according to Claim [8] 9 which is an HPV16 E1 protein.

11. A polynucleotide according to Claim 10 which comprises the polynucleotide of FIGURE 2 (SEQ. ID.NO:2).

[12. A polynucleotide according to Claim 4 wherein the protein is E2 protein or a mutated E2 protein and is from an HPV selected from the group consisting of: HPV6a, HPV6b, HPV11, HPV16, HPV18, HPV31, HPV33, HPV35, HPV39, HPV45, HPV51, HPV52, HPV56, HPV58, and HPV 68.]

13. (Amended) A polynucleotide according to Claim [12] 4 wherein the protein is a mutated E2 protein.

14. (Amended) A polynucleotide according to Claim [11] 13 which is an HPV16 E2 mutated protein.

15. A polynucleotide according to Claim 14 which comprises the polynucleotide of FIGURE 3 (SEQ. ID.NO: 3).

[16. A polynucleotide according to Claim 4 wherein the protein is E7 or an E7 mutant and is from an HPV selected from the group consisting of: HPV6a, HPV6b, HPV11, HPV16, HPV18, HPV31, HPV33, HPV35, HPV39, HPV45, HPV51, HPV52, HPV56, HPV58, HPV68.]

17. (Amended) A polynucleotide according to Claim [16] 4 wherein the protein is an HPV[6a]16E7 protein.

18. A polynucleotide according to Claim 17 which comprises the polynucleotide of FIGURE 4 (SEQ. ID.NO:4).

19. (Amended) An adenoviral vaccine vector comprising an adenoviral genome with a deletion in the E1 region, and an insert in the E1 region, wherein the insert comprises an expression cassette comprising:

A) a polynucleotide encoding a[n] codon-optimized HPV16 protein selected from the group consisting of L1, E1, E2, and E7 proteins or mutant forms thereof, wherein [the] said polynucleotide is codon-optimized for expression in a human host cell; and

B) a promoter operably linked to the polynucleotide.

20. A vector according to Claim 19 wherein the adenoviral genome also contains a deleted E3 region.

21. (Amended) A shuttle plasmid vector comprising a plasmid portion and an adenoviral portion, the adenoviral portion comprising: an adenoviral genome with a deletion in the E1 region, and an insert in the E1 region, wherein the insert comprises an expression cassette comprising:

A) a polynucleotide encoding a[n] codon-optimized HPV16 protein selected from the group consisting of L1, E1, E2, and E7 proteins, wherein [the] said polynucleotide is codon-optimized for expression in a human host cell; and

B) a promoter operably linked to the polynucleotide.

22. (Amended) A vaccine plasmid comprising a plasmid portion and an expression cassette portion, the expression cassette portion comprising:

A) a polynucleotide encoding a[n] codon-optimized HPV16 protein selected from the group consisting of L1, E1, E2, and E7 proteins, wherein [the] said polynucleotide is codon-optimized for expression in a human host cell; and

B) a promoter operably linked to the polynucleotide.

23. (Amended) A plasmid according to Claim 22 wherein the plasmid portion is V1Jns.

24. (Amended) A method for inducing immune responses in a vertebrate which comprises administering to a vertebrate subject [introducing] between 1 ng and 100 mg of the composition [polynucleotide] of Claim 1 [into the tissue of] to the vertebrate.

25. (Amended) A method for inducing immune responses in a vertebrate which comprises administering to a vertebrate subject [introducing] between 10^{11}-10^{12} particles of an adenoviral vector carrying the composition [polynucleotide] of Claim 1 [into the tissue of] to the vertebrate.

26. (Amended) A method for inducing an immune response against human papillomavirus in a vertebrate, comprising

A) administering to a vertebrate subject [introducing into the vertebrate] a first vector comprising a polynucleotide encoding a[n] codon-optimized HPV16 protein selected from the group consisting of L1, E1, E2, and E7 proteins, wherein [the] said polynucleotide is codon-optimized for expression in a human host cell;

B) allowing a predetermined amount of time to pass; and

C) administering to said vertebrate subject [introducing into the vertebrate] a second vector comprising adenoviral vaccine vector comprising an adenoviral genome with a deletion in the E1 region, and an insert in the E1 region, wherein the insert comprises an expression cassette comprises

i) a polynucleotide encoding a[n] codon-optimized HPV16 protein selected from the group consisting of L1, E1, E2, and E7 proteins or mutant forms thereof, wherein [the] said polynucleotide is codon-optimized for expression in a human host cell; and

ii) a promoter operably linked to the polynucleotide.

27. A method according to Claim 26 wherein the vertebrate is human.

28. (Amended) A method for inducing immune responses in a vertebrate comprising

A) administering to a vertebrate subject [introducing into the vertebrate] a plasmid vaccine, wherein the plasmid vaccine comprises a plasmid portion and an expression cassette portion, the expression cassette portion comprising:

i) a polynucleotide encoding a[n] codon-optimized HPV16 protein selected from the group consisting of L1, E1, E2, and E7 proteins, wherein [the] said polynucleotide is] codon-optimized for expression in a human host cell; and

ii) a promoter operably linked to the polynucleotide;

B) allowing a predetermined amount of time to pass; and

C) administering to said vertebrate subject [introducing into the vertebrate] an adenoviral vaccine vector comprising an adenoviral genome with a deletion in the E1 region, and an insert in the E1 region, wherein the insert comprises an expression cassette comprising:

i) a polynucleotide encoding a[n] codon-optimized HPV16 protein selected from the group consisting of L1, E1, E2, and E7 proteins or mutant forms thereof, wherein [the] said polynucleotide is codon-optimized for expression in a human host cell; and

ii) a promoter operably linked to the polynucleotide.

29. A method according to Claim 28 wherein the vertebrate is human.

30. (Amended) A method of making a codon-optimized HPV16 protein comprising expressing in a human host cell a synthetic polynucleotide encoding a human papillomavirus serotype 16 (HPV16) protein, or mutated form thereof [a HPV protein] which has reduced protein function for viral replication and cellular transformation as compared to wild-type protein, but which maintains immunogenicity, wherein said polynucleotide sequence comprises[ing] codons optimized for expression in a human host.